L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
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TI Preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity
IN Acton, John J., III; Meinke, Peter T.; Wood, Harold B.; Black, Regina M.
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	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2495915	A1	20040311	CA 2003-2495915	20030828
	AU 2003260085	A1	20040319	AU 2003-260085	20030828
	EP 1546142	A2	20050629	EP 2003-791782	20030828
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	US 2005272788	A1	20051208	US 2005-525470	20050224 <--
PRAI	US 2002-406737P	P	20020829		
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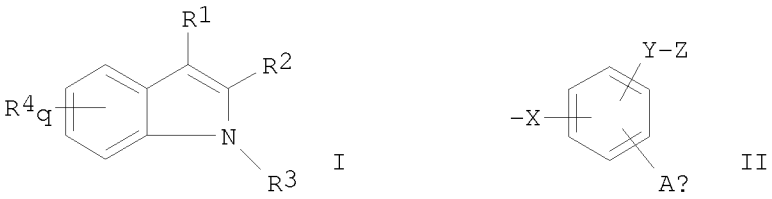
GI



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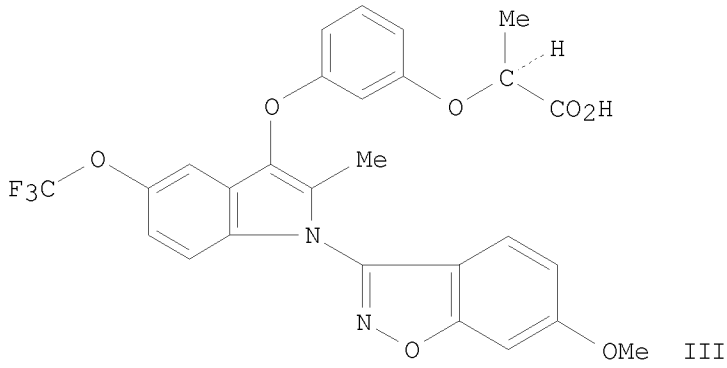

III

AB Indoles having aryloxyalkanoic acid substituents or arylalkanoic acid substituents are agonists or partial agonists of PPAR gamma and are useful in the treatment and control of hyperglycemia that is symptomatic II diabetes, as well as dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and obesity that are often associated with type 2 diabetes. Indoles having aryloxyalkanoic acid or arylalkanoic acid substituents (shown as I; variables defined below; e.g. III) are agonists or partial agonists of PPARγ and are useful in the treatment and control of hyperglycemia that is symptomatic of type 2 diabetes, as well as dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and obesity that are often associated with type 2 diabetes. Compds. I have EC50 = 1-3000 nM in Gal-4 hPPAR transactivation assays (no data for individual compds. are given). For I: R1 is II wherein X = a bond, O, S(O)n, CO, CH2, CHMe, CMe2, and C3-6cycloalkylidene; Y = -CH:CH-, -CH(OH)CH(OH)-, -OCR7R8-, -SCR7R8-, and -CH2CR5R6-; Z = -CO2H and tetrazole; A = H, C1-4 alkyl, C1-4 alkenyl, -O1-4-alkyl, and halogen, wherein alkyl, alkenyl, and Oalkyl are (un)substituted with 1-5 halogens. R5, R6, R7, and R8 = H, halogen, C1-C5 alkyl, OC1-C5 alkyl, C2-C5 alkenyl, OC2-C5 alkenyl, C3-6 cycloalkyl, (CH2)0-2phenyl, -O(CH2)0-2phenyl and CO2H, wherein C1-C5 alkyl, OC1-C5 alkyl, C2-C5 alkenyl, OC2-C5 alkenyl, C3-6 cycloalkyl, and Ph are (un)substituted with 1-5 halogens, and C3-6 cycloalkyl and Ph are further (un)substituted with 1-3 C1-C3 alkyl and OC1-C3 alkyl, said C1-C3 alkyl and OC1-C3 alkyl being (un)substituted with 1-3 halogens; or R7 and R8 may be connected to form a C3-C6 cycloalkyl group, said C3-C6 cycloalkyl being (un)substituted with 1-3 halogens; or, when Y is OCR7R8, R8 may optionally be a 1-2-C bridge connected to the Ph ring at the position ortho to Y, thereby yielding a 5 or 6-membered heterocyclic ring fused to the Ph ring. R2 is C1-C4 alkyl, which is (un)substituted with 1-5 halogens; R3 = 3-benzisoxazolyl, 3-benzisothiazolyl, and 3-benzpyrazolyl, wherein R3 is (un)substituted with 1-3 halogen, C1-3alkyl, and OC1-3alkyl, wherein C1-3alkyl and OC1-3alkyl are (un)substituted with 1-5 halogens; each R4 = halogen, C1-C3 alkyl, and OC1-C5 alkyl, wherein C1-C3 alkyl and OC1-C5 alkyl are (un)substituted with 1-5 halogens; n = 0-2; p = 0-3; and q = 0-3. Although the methods of preparation are not claimed, 11 example prepns. are included. For example, III was prepared in 8 steps starting with

substitution of chloroacetone with 3-benzoyloxyphenol to give 1-(3-hydroxyphenoxy)-2-propanone followed by cyclization with 4-trifluoromethoxyphenylhydrazine hydrochloride to give 3-(3-hydroxyphenoxy)-2-methyl-5-(trifluoromethoxy)-1H-indole, followed by O-protection, followed by substitution at N with 3,6-dichloro-1,2-benzisoxazole, followed by deprotection at O, followed by etherification with iso-Bu (R)-lactate, followed by base hydrolysis of the ester functionality, followed by substitution of MeO for Cl.